

PATENT  
USSN 09/432,503  
015389-002611US; 018/063c

### REMARKS

Claims 41-91 are currently pending in this application, and under examination.

The Advisory Action dated March 19, 2004, indicates that the Amendment under 37 CFR § 1.116 filed February 26, 2004, has been entered into the case, for which applicants are grateful. Applicants also gratefully acknowledge withdrawal of the double patenting rejection. Claims 42, 45-46, 49, 52-55 and 57 are allowed. Claims 41 and 48 are objected to, and the other claims stand rejected.

Entry of this Amendment and reconsideration of the application is requested under 37 CFR § 1.114(c).

### Interview summary

The undersigned is grateful to Examiner Delia M. Ramirez, Examiner Rebecca Prouty, and Practice Specialist Brian Stanton, for the interview held at the Patent Office on March 11, 2004.

The patentability of the claimed invention as it relates to use *in vivo* was discussed extensively. Applicants agreed to file this RCE, with the understanding that the arguments presented in the Response filed February 26, 2003 will be reconsidered by the Office. Brian Stanton undertook to consult with other examiners knowledgeable in the field of gene therapy, and to assist Examiner Ramirez in determining what coverage for *in vivo* use applicants were entitled to. It was agreed that the filing of this Interview Summary with the RCE would prevent the next Action from being made final. However, applicants reserve their right to reinitiate the appeal if needed to obtain adequate coverage for commercially important embodiments of the invention.

A summary of the issues to be reconsidered with respect to the description and enablement rejections is provided on page 9, below.

### Claim amendments

Claims 43-44, 47, 50-51, and 56 are amended in a manner that is believed to overcome the rejection made under 35 USC § 112 ¶ 2. Claims 41, 48, 58, and 61 have been amended in the manner recommended in the Advisory Action. Applicants thank the Examiner for these suggestions. Claims 49-51 and 53-57 have also been amended to add some useful commas. These amendments do not add new matter to the disclosure.

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Claims 69, 78, and 87 stand rejected under § 112 ¶ 2 because the Examiner was not able to find support for telomerized endothelial cells. The Examiner is respectfully referred to page 53: lines 17-18; page 113: lines 26-27; page 123: lines 15-19; and page 123: line 41. This application is a continuation of issued U.S. Patent 6,166,178, which can be searched and reviewed electronically.

The Advisory Action indicates that the claims in the Amendment filed February 26, 2004 do not match those pending in the application on April 21, 2003. Applicants apologize for any confusion in this matter. Claims 41-91 listed above reflect the claim set presented on February 26, 2004, as reviewed in the Advisory Action of March 19, 2004, and amended herein.

Applicants respectfully request that the application proceed based on the claims as listed above. If the Examiner would like a further delineation of the difference between these claims and a previous version, or if any other action is appropriate to continue prosecution with the current claim set, the Office is requested to notify applicants accordingly.

Patentability of claims related to use *in vivo*

Claims 58-91 stand rejected under both the written description and enablement requirements of 35 USC § 112 ¶ 1. The Office Action dated June 18, 2003, and the Advisory Action dated March 19, 2004, indicates that the specification is enabling for increasing proliferative capacity of a cell *in vitro*, but does not describe or enable use of TRT to increase proliferative capacity of a cell *in vivo*.

Applicants respectfully disagree for reasons previously indicated. Applicants submit that the invention is described and enabled for use *in vivo*, for example, using commonly used gene therapy vectors, such as *adenovirus* (claim 63) and *retrovirus* (claim 64).

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The Office is respectfully requested to consider the following points:

- The Office has already agreed that the specification is generally enabling for the use of TRT to increase replicative capacity of mammalian cells *in vitro*. The only question is whether a different result would be expected if a TRT polynucleotide is introduced into a cell *in vivo*.
- The specification extensively describes the use of TRT for purposes of gene therapy (page 110, line 29 ff.), and to increase proliferative capacity of cells (page 118, line 22 ff.).
- Preferred vectors are listed in the specification on page 66, line 5 ff. The first two vectors listed are *adenovirus* and *retrovirus*. The use of adenovirus for increasing cell replicative capacity is illustrated on page 246, line 30 ff.
- The Response filed February 26, 2003, explains how the specification meets the legal requirements for written description and enablement, according to current case law.
- The 37 CFR § 1.132 Declaration by Dr. Calvin Harley explains that successful introduction of the TRT vector *in vivo* should increase the proliferative capacity of cells, *the same way it does in vitro*.
- The publication by Rudolph et al. (Science 287:1253-1257) "Inhibition of Experimental Liver Cirrhosis in Mice by Telomerase Gene Delivery" referred to in the Harley Declaration shows that TRT gene therapy can be used to restore telomerase function in a mouse model for liver cirrhosis, attributable to increased cell survival and proliferation.
- Dr. Harley also explains that experiments done in the art-accepted rabbit model for ischemic wounds shows that TRT improved perfusion in ischemic tissue, attributable to an increase in proliferative capacity of the cells *in vivo*.
- The 37 CFR § 1.132 Declaration by Dr. John Irving explains how someone reading this application at the time it was filed would know how to construct gene therapy vectors (particularly retrovirus and adenovirus vectors) — *such as those used in the rabbit model experiments described by Dr. Harley*.
- The Response filed February 26, 2003 lists scientific publications confirming the utility of adenovirus and retrovirus gene therapy vectors for a number of different cell types (other illustrations are available upon request)

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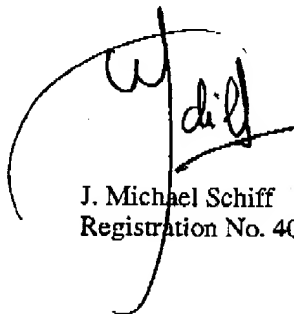
Request for further interview

Applicants respectfully request that all outstanding rejections be reconsidered and withdrawn. The application is believed to be in condition for allowance, and a prompt Notice of Allowance is requested.

If after internal review, the Office is still not able to resolve the issue regarding the use of the claimed invention *in vivo*, applicants hereby request a further interview. Please contact applicants' representative at the telephone number indicated below.

Should the Patent Office determine that a further extension of time or any other relief is required for further consideration of this application, applicants hereby petition for such relief. The Commissioner is hereby authorized to charge the cost of such petitions and other fees due in connection with the filing of these papers to Deposit Account No. 07-1139.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "J. Michael Schiff", is written over a large, stylized, handwritten "J" that spans across the signature and the name below it.

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